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Amendment And Reply

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carrier, and p-glycoprotein. Cell deposited in National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, the Ministry of International Trade and Industries, under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure, under the deposition number FERM BP-6507 can be given as such established cells.

*B1*  
*cancel*  
Please replace the paragraph at page 10, lines 8 through 19 with the following paragraph:

*B2*  
The present invention also relates to established cells derived from choroid plexus epithelial cells of such a transgenic animal. Specifically, the present invention relates to established cells expressing a temperature sensitive SV40 large T-antigen gene, showing localization of  $\text{Na}^+ - \text{K}^+$  ATPase and GLUT-1 transport carriers in the cell membrane, and when cultured in a monolayer, showing the localization of  $\text{Na}^+ - \text{K}^+$  ATPase in the apical side. The cells deposited in National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, the Ministry of International Trade and Industries, under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure, under the deposition number FERM BP-6508 can be given as such established cells.

Please replace the paragraph at page 11, lines 15 through 26 with the following paragraph:

*B3*  
Furthermore, the present invention relates to established cells derived from brain capillary endothelial cells of such a transgenic animal. Specifically, the present invention relates to established cells which express a temperature sensitive

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SV40 large T-antigen, maintain an alkaline phosphatase activity and  $\gamma$ -glutamyltransferase activity, and express a scavenger receptor, GLUT-1 transporter and p-glycoprotein. The cell line deposited in National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, the Ministry of International Trade and Industries, under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure, under the deposition number FERM BP-6873 can be given as such an established cell.

*B3  
Cerv*

Please replace the paragraph at page 20, lines 1 through 27 with the following paragraph:

by being together in a cage. The ova at pronucleous stage were collected at 32 hours after the hCG administration by oviduct perfusion. A mKRB solution (Toyoda Y. and Chang M.C., J. Reprod. Fertil., 36, 9-22 (1974)) was used for the oviduct perfusion and incubation of ova. The collected (fertilized) ova were treated by an enzyme in an mKRB solution containing 0.1% hyaluronidase (Hyaluronidase TypeI-S, made by Sigma Co.) at 37°C for 5 minutes to remove cumulus cells. After washing three times with the mKRB solution to remove the enzyme, the fertilized ova were stored in a CO<sub>2</sub> incubator (5% CO<sub>2</sub>-95% air, 37°C, saturated humidity) until DNA microinjection. A DNA solution was microinjected into the male pronucleus of the rat (fertilized) ova thus prepared. 228 ova after microinjection were transplanted in nine recipients (foster mothers) and 80 pups were obtained. The integration of the DNA was analyzed with DNA prepared from tails of the rats immediately after weaning by the PCR method (primers used: tsA58-1A, 5'-TCCTAATGTGCAGTCAGGTG-3', SEQ ID NO:1 (corresponds to 1365-1384 sites), tsA58-1B, 5'-TGACGAGCTTGGCACTTG-3', SEQ ID NO:2 (corresponds to 1571-1590 sites)). As a result, 20 rats (6 male, 8 female, and 6 unknown sexuality) were identified to have the gene introduced.

*DK*

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*B4  
carried  
B6*

Among these rats, 11 transgenic rat lines (male lines: #07-2, #07-5, #09-6, #12-3, #19-5, female lines: #09-7, #11-6, #12-5, #12-7, #18-5, #19-8) which survived as long as 12 weeks after elapse of the sexual maturation period were obtained. These G0 generation transgenic rats were mated with Wistar rats and established 2 lines of male founders (#07-2, #07-5) and 3 lines

Please replace the paragraph at page 23, lines 5 through 8 with the following paragraph:

*B6*

TR-iBRB2 was deposited in National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, the Ministry of International Trade and Industries, under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure. The deposition number is FERM BP-6507.

Please replace the paragraph at page 31, lines 5 through 8 with the following paragraph:

*B6*

TR-CSFB3 was deposited in National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, the Ministry of International Trade and Industries, under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure. The deposit number is FERM BP-6508.

Please replace the paragraph at page 47, lines 3 through 4 with the following paragraph:

*B6*

Name and address of the organization in which the microorganisms have been deposited under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure:

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Please replace the paragraph at page 47, lines 14 through 15 with the following paragraph:

*B8*  
Name and address of the organization in which the microorganisms have been deposited under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure:

Please replace the paragraph at page 47, lines 25 through 26 with the following paragraph:

*B9*  
*B10*  
Name and address of the organization in which the microorganisms have been deposited under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure:

Please replace the Abstract at page 52, lines 3 through 25 with the following Abstract:

*B10*  
Established cells derived from retinal capillary endothelial cells, choroid plexus epithelial cells, or brain capillary endothelial cells or a transgenic animal carrying a large T-antigen gene of an SV40 temperature sensitive mutant tsA58 are disclosed. The cell line derived from retinal capillary endothelial cells expresses a temperature sensitive SV40 large T-antigen, GLUT-1 transporter, and p-glycoprotein. The cell line derived from choroid plexus epithelial cells expresses a temperature sensitive SV40 large T-antigen gene and shows localization of  $\text{Na}^+ - \text{K}^+$  ATPase and GLUT-1 transporter in the cell membrane. When cultured in a monolayer, it shows the localization of  $\text{Na}^+ - \text{K}^+$  ATPase in the